A BRIEF REVIEW OF THE THYREOID THEORY IN GRAVES' DISEASE.—REPORT OF TWO CASES TREATED BY THYREOIDECTOMY.[1]

By J. ARTHUR BOOTH, M. D.

RECENT investigations as to the functions of the thyreoid gland and the internal administration of the extract of the thyroid in the treatment of myxœdema, as well as the increasing number of cases reported as cured by operation, affords material for further reflection, and certainly encourages one to renewed labor in the study of the etiology and pathology of the symptom-complex so well known by the designation of Graves' disease. During the past three years the German surgeons have reported quite a number of typical cases of this disease, cured by partial removal of the thyroid and although here in America the sentiment in favor of operative interference in these patients is slow in its growth, still facts are accumulating which inclines one to believe that a cure is possible by thyroidectomy.

Although any of the various theories which have been advanced with regard to the origin of this mysterious disease are satisfactory in explanation of individual symptoms, none seem sufficient to account for the entire complex presented by it. A focal nerve lesion in the symphathetic or medulla certainly does not explain the condition, and it does seem that there must be something more than a simple neurosis.

The antithesis presented by myxœdema, and the successful treatment of the same, as well as the more careful investigation of the pathological changes in the thyroid, have, within recent years, resulted in the advancement of a new theory, which is founded on the supposition that exophthalmic goitre may be due to a primary disease of the thyroid gland, and through functional or structural change causes some poison to be generated here, which, circulating in the blood, irritates the nerves; or that it withdraws from the blood too much of certain substances needed for nerve nutrition. In speaking of it as a disease of the thyroid, it is not to be understood that a nervous causation is to be entirely excluded. Grutzner, from physiological experiments, concludes that the thyroid has the function of neutralizing certain products of the economy harmful to the nervous system. If the blood of an animal, from which the thyroid has been previously extirpated, is infused into the veins of another animal, the latter shows symptoms similar to those of operative myxœdema in man. Furthermore, it is an interesting fact that during the application of the thyroid treatment many symptoms are produced that are similar to those found in Graves' disease, viz, tachycardia, elevation of temperature, insomnia, agitation, polyuria, incomplete paraplegia, excessive sweating and diarrhœa.

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[1] Read at the meeting of the American Neurological Association, Washington, D. C., May 30, 1894.

The thyroid theory is supported by the similarity and points of contrast between this disease and others depending upon a deficient action of the thyroid, by the fact that signs of Graves' disease may develop in cases of ordinary goitre, and that operative treatment may influence the disease considerably. It is not necessary to repeat the many facts in support of these dicta already often recorded and now accepted both here and abroad.

Quite a number of objections have been raised which are thought to weaken this theory, and among these the following deserve consideration:

1. Tachycardia and many other characteristic symptoms may develop without a goitre.

2. In simple enlargement of the thyroid the symptoms of Graves' disease do not appear.

3. Exophthalmos and Græfe's sign have not been produced in those cases of myxœdema treated by the internal administration of the thyroid.

Concerning this first objection, there is a doubt whether, in all the cases so reported, a careful and thorough examination was made for slight enlargements of the gland, and though not found by inspection and palpation, it does not mean that there may not be a slight increase in size or change of structure. It is exceedingly difficult to determine its exact size during life, and in the thyroidectomy cases it is surprising to find how much larger the gland really is when exposed to view. Even if there be no increase in size, there may be perverted function, causing, possibly, direct irritation of the muscle of the heart; for recent pathological investigation has demonstrated special changes in the amount of secreting tissue in these cases. Greenfield, of Edinburgh, especially emphasizes the point that it is not the mere size of the gland which is of importance, but its structural alterations. In order to verify these suppositions, the thyroid in future should receive more attention than it has in the past.

(2) The second statement may be true as to a certain number of cases, but there are also some of this class who do develop tachycardia and many of the nervous symptoms of Graves' disease. Besides, in cases of simple goitre, we are not sure that enlarged thyreoid necessarily means altered function.

(3) Regarding the absence of exophthalmos in those cases treated by the internal administration of the thyroid, we now know that many of the minor symptoms have been produced, and it is now important to inquire whether exophthalmos might not result if it were possible to push the medication to a greater degree without danger.

Although we cannot, at this time, answer positively all these mooted points and arrive at any dogmatic conclusion, still, when we stop to consider the present state of our knowledge of the disease and the results obtained by treatment, we must certainly confess that a marked advance has been made, further corroborative pathological findings being only necessary in order to make the thyroid gland the responsible nucleus for this interesting disease.

As additional evidence of the improvement to be obtained by partial removal of the thyroid, I now wish to record the following cases;

CASE I.—The patient, Louis E., aged 24, was first seen January 23, 1893. The family history is entirely negative. She never had any illness worthy of note up to the date of the present trouble. About two years ago she first noticed enlargement of the neck, and three months later the eyes became affected. The patient is positive that there were no heart symptoms until six months later, when palpitation, throbbing in the vessels of the neck, shortness of breath and flushing of the face appeared. All these symptoms gradually increased in severity, and in addition there was marked insomnia, because of the tumultuous action of the heart. Both eyes are very prominent, especially the left, and the lids do not follow the movements of the eyeballs. The pupils are moderately dilated, reacting to light and accommodation. Vision not impaired and fundus normal.

The enlargement of the thyreoid is marked; the right lobe being the larger. On inspection, pulsation is quite noticeable over this region along the sides of the neck. Over the middle of the thyreoid, the neck measures 14 inches. The pulse is 150 and of high tension. The apex beat is diffused, but no murmur is present. Respirations 24 to the minute. Measurement over bust 31½ inches, and on full inspiration 32¼. During a period of six months, from January to July, 1893, the patient received daily applicatious of galvanism and appropriate internal medication. At the end of the above period there was some improvement in all the symptoms, including a slight reduction in the size of the neck, and the eyes were less prominent. During July, August and September, the patient received no regular treatment, but faithfully carried out my instructions as to resting several hours each day. After this time, she relapsed into her former condition; the exophthalmos was well marked, and the right lobe of the thyreoid very prominent. Further treatment failed to make any material alteration in her appearance, or cure the many subjective symptoms from which she suffered; so operative interference was considered and decided upon. The accompanying photographs Nos. 1 and 2 show fairly well the appearance of the patient at this time.

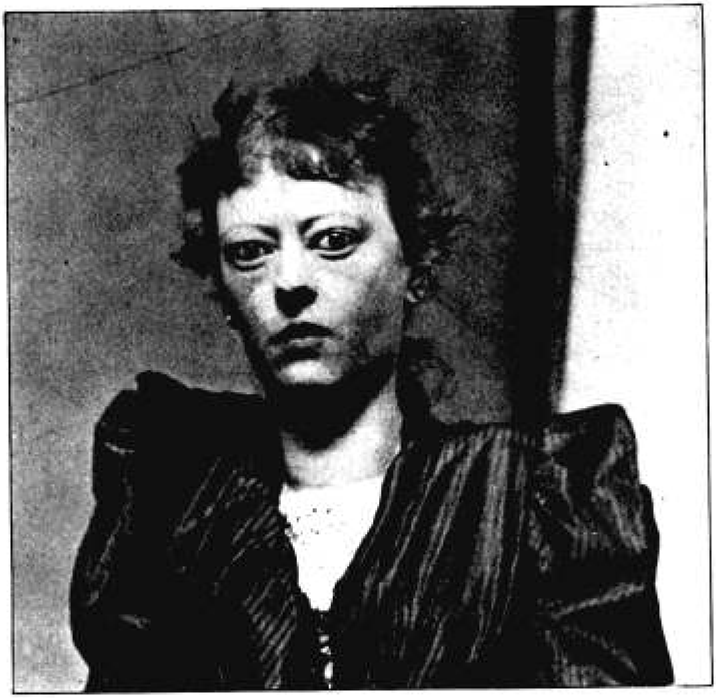

FIG. 1.

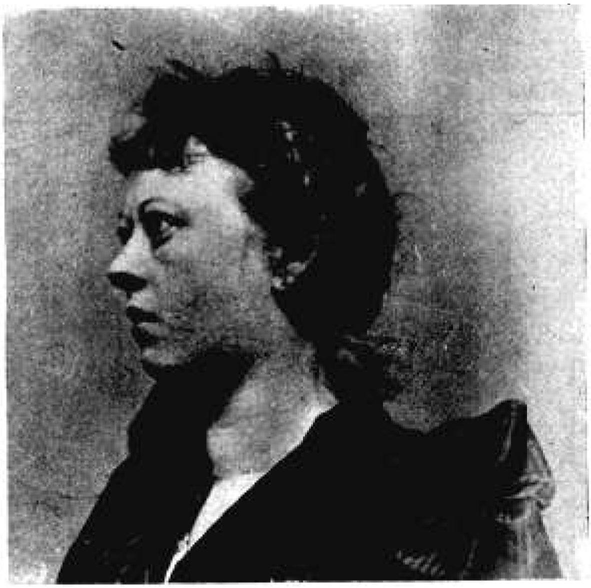

FIG. 2.

The operation was performed by Dr. B. F. Curtis, on November 11, 1893. A right transverse incision was made just below the hyoid bone and a vertical incision from the inner end of this at median line. The flap thus made was turned back and exposed the right lobe of the thyreoid. There was but little bleeding, the vessels being carefully dissected out and tied as found. A supernumary lobe was found attached to the inferior angle and pressing directly upon the trachea; this was removed. The entire exposed mass was then separated from its bed and from the trachea, the isthmus ligated and the whole right lobe removed.

During the operation, the pulse was between 180 and 200, irregular and intermittent, but respiration continued normal and no stimulation was necessary. By evening she had made a good recovery from the ether, complaining of severe pain in the throat. Voice not husky and of good strength. Up to the fourth day after the operation, nothing occurred worthy of note; the patient then had much nausea and vomiting, accompanied by a sharp rise in temperature. These symptoms continued for two days and then rapidly disappeared. On the tenth day, the dressing was removed for the first time, and the wound was found healed by primary union.

The course of the case after this was satisfactory, and on the sixteenth day she was discharged from the hospital.

Inspection of the specimen after removal did not reveal any great degree of vascularity; it was homogenious in appearance and hard in consistency. Microscopically, the tissue showed the structure of normal thyreoid gland with the alveoli moderately distended with hyaline material, and in places thickly crowded small cells, both in the alveoli and in the stroma, but principally in the latter.

It is now about seven months since the operation, and there has been a progressive and decided improvement in all the symptoms, especially is this so with regard to the various nervous phenomena, viz., insomnia, restlessness, flushing of the face, excessive sweating and palpitation. The pulse now varies between 96 and 110, as compared to the former ratio of 120 to 160. The appended table shows the pulse average of the past nine months.

AVERAGE OF PULSE RATE.

1893	August	148
	September	156
	October	136
	November	146
	December	120

1894	January	120
	February	110
	March	104
	April	104

Operation—November 11, 1893.

The eyes are noticeably less prominent, and the remaining left lobe of the thyreoid is smaller; the degree of improvement being appreciated by comparing these photographs taken at different intervals before and since the operation.

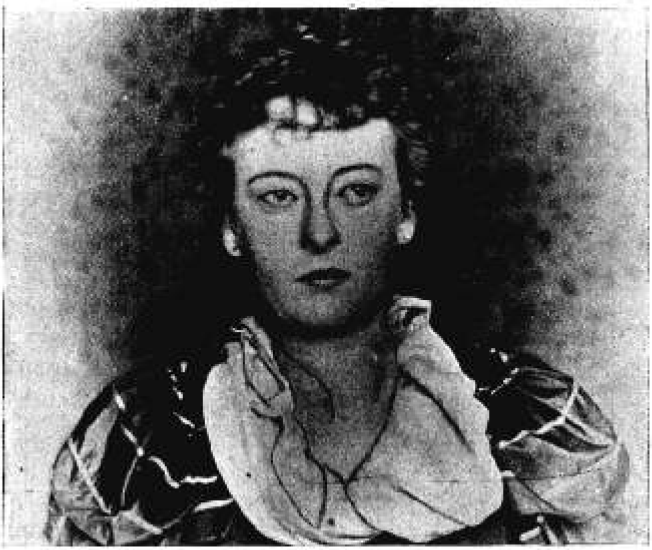

FIG. 3

CASE II.—Anna D——, *æt.* 20, single. One month ago (April 23d), the patient was referred to me by Dr. S. E. Milliken, and the following history obtained: Family history negative. Three years ago, she first noticed the enlargement of her neck, and three months later prominence of both eyes. She became very nervous, could not sleep, and was much disturbed by frequent attacks of palpitation.

The tumor in the neck gradually increased in size, and on May 11, 1893, she entered Roosevelt Hospital, where a few days later the right lobe of the thyreoid was removed by Dr. McBurney.

Six months after the operation, the nervous symptoms had entirely disappeared, the eyes became less prominent, and there were no attacks of palpitation or dyspnœa.

It is now one year since the operation, and there is entire absence of any exophthalmos; the pulse, formerly 140, is at present below 100 beats to the minute, and the nervous symptoms have disappeared.

We must confess from the facts before us that the results obtained in these two cases are in additional support of the evidence already introduced by Wette, Mobius, Joffroy, Greenfield and Putnam.

Conclusions: 1. It is by no means decided that a mere excess of the thyreoid secretion is the sole and essential factor in Graves' disease; but as microscopical examination has demonstrated an enormous hyperplasia of the secreting structure, it is certainly reasonable to suppose that these changes must have some profound effect, both on the quality and quantity of the secretion.

2. If altered structure and not size is the test of the disease, then thyreoidectomy should be considered even in those cases where there is little or no enlargement of the thyreoid.

3. Cases of Graves' disease may be entirely cured by thyreoidectomy.

How this is brought about is not clear as yet. It may be in one of three ways, viz., a diminution of the functional activity of the gland substance; a relief of the stretching and irritation of the sympathetic nerve fibres, or, finally, in the removal of pressure.